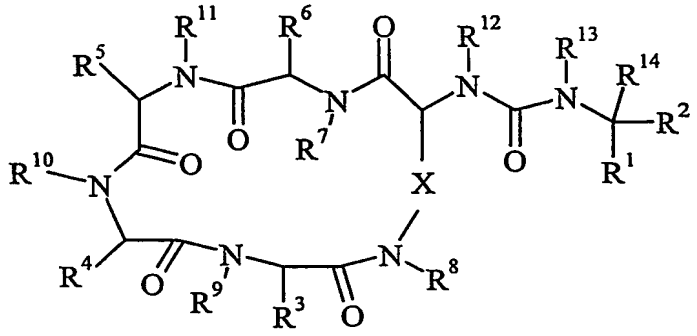
CLAIMS

1. The use of a compound of formula (I):



(I)

wherein:

X is $(CH_2)_mY(CH_2)_n$;

m and n are, independently, 1, 2, 3, 4, 5 or 6; provided that m + n is not more than 6;

Y is a bond, O, $S(O)_p$, or S-S;

R^1 is CO_2R^{15} or a carboxylic acid isostere such as $S(O)_2OH$, $S(O)_2NHR^{15}$, $PO(OR^{15})OH$, $PO(OR^{15})NH_2$, $B(OR^{15})_2$, $PO(R^{15})OH$, $PO(R^{15})NH_2$ or tetrazole;

R^2, R^3, R^4, R^5 and R^6 are, independently, hydrogen, C_{1-6} alkyl (optionally substituted by halogen, hydroxy, cyano, SH, $S(O)_3H$, $S(O)_q(C_{1-6}$ alkyl), $OC(O)(C_{1-4}$ alkyl), CF_3, C_{1-4} alkoxy, OCF_3, COOH, $CONH_2$, $CONH(C_{1-6}$ alkyl), NH_2, $CNH(NH_2)$, or $NHCNH(NH_2)$), C_{3-6} cycloalkyl(C_{1-4})alkyl (wherein the cycloalkyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$), heterocyclyl(C_{1-4})alkyl (wherein the heterocyclyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$), phenyl(C_{1-4})alkyl (wherein the phenyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$) or heteroaryl(C_{1-4})alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$);

p and q are, independently, 0, 1 or 2;

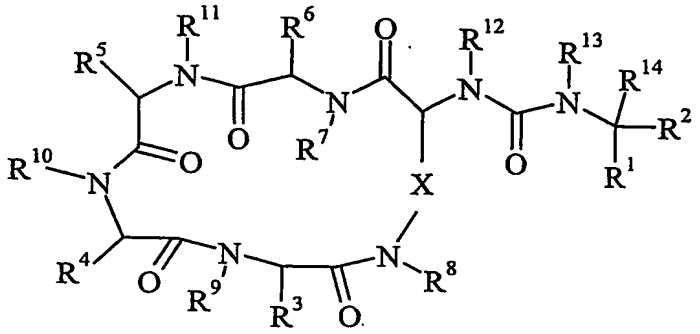
R^7, R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} are, independently, H or C_{1-4} alkyl;

R^{14} is H or C_{1-4} alkyl; and,

R^{15} is H or C_{1-4} alkyl;

or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt; in a method of manufacturing a medicament for the treatment or prophylaxis of a condition wherein inhibition of carboxypeptidase U is beneficial.

2. A compound of formula (I):



(I)

wherein:

X is $(CH_2)_4$;

R^1 is CO_2R^{15};

R^2 is straight-chain C_{1-6} alkyl substituted at its terminus by NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; C_{3-6} cycloalkyl substituted by NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; heterocyclyl containing at least one nitrogen atom; non-nitrogen containing heterocyclyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; heteroaryl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; phenyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; heteroaryl(C_{1-4})alkyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; phenyl(C_{1-4})alkyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; or C_{3-6} cycloalkyl(C_{1-4})alkyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; all of the above rings being optionally further substituted by one or more of: halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy or OCF_3;

one of R^3, R^4, R^5 and R^6 is independently, hydrogen, heteroaryl(C_{1-4})alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$); and the others are, independently, hydrogen, C_{1-6} alkyl (optionally substituted by halogen, hydroxy, cyano, SH, $S(O)_3H$, $S(O)_q(C_{1-6}$ alkyl), $OC(O)(C_{1-4}$ alkyl), CF_3, C_{1-4} alkoxy, OCF_3, COOH, $CONH_2$, $CONH(C_{1-6}$ alkyl), NH_2, $CNH(NH_2)$, or $NHCNH(NH_2)$), C_{3-6} cycloalkyl(C_{1-4})alkyl (wherein the cycloalkyl ring is optionally substituted by halogen,

hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$), heterocyclyl(C_{1-4})alkyl (wherein the heterocyclyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$), phenyl(C_{1-4})alkyl (wherein the phenyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$) or heteroaryl(C_{1-4})alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$);

p and q are, independently, 0, 1 or 2;

R^7, R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} are, independently, H or C_{1-4} alkyl;

R^{14} is H or C_{1-4} alkyl; and,

R^{15} is H or C_{1-4} alkyl;

or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt.

3. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt. as claimed in claim 2 wherein:

X is $(CH_2)_4$;

R^1 is CO_2R^{15};

R^2 is straight-chain C_{1-6} alkyl substituted at its terminus by NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; C_{3-6} cycloalkyl substituted by NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; heterocyclyl containing at least one nitrogen atom; non-nitrogen containing heterocyclyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; heteroaryl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; phenyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; heteroaryl(C_{1-4})alkyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; phenyl(C_{1-4})alkyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; or C_{3-6} cycloalkyl(C_{1-4})alkyl substituted with NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; all of the above rings being optionally further substituted by one or more of: halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy or OCF_3;

one of R^3, R^4, R^5 and R^6 is independently, hydrogen, heteroaryl(C_{1-4})alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$); and the others are, independently, hydrogen, C_{1-6} alkyl (optionally substituted by halogen, hydroxy, cyano, SH, $S(O)_3H$, $S(O)_q(C_{1-6}$ alkyl), $OC(O)(C_{1-4}$ alkyl), CF_3, C_{1-4} alkoxy, OCF_3, COOH, $CONH_2$, $CONH(C_{1-6}$

alkyl), NH_2, $CNH(NH_2)$, or $NHCNH(NH_2)$), C_{3-6} cycloalkyl(C_{1-4})alkyl (wherein the cycloalkyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$), heterocyclyl(C_{1-4})alkyl (wherein the heterocyclyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$), phenyl(C_{1-4})alkyl (wherein the phenyl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$) or heteroaryl(C_{1-4})alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C_{1-4} alkyl, CF_3, C_{1-4} alkoxy, OCF_3, NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$);

p and q are, independently, 0, 1 or 2;

R^7, R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} are, independently, H or C_{1-4} alkyl;

R^{14} is H or C_{1-4} alkyl; and,

R^{15} is H or C_{1-4} alkyl;

or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt.

4. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt as claimed in claim 2 or 3 wherein:

R^1 is CO_2R^{15};

R^2 is straight-chain C_{1-6} alkyl substituted at its terminus by NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; C_4 alkyl (such as $CH(CH_3)CH_2CH_3$ or $CH_2CH(CH_3)_2$); or (aminopyridinyl)methyl (for example (6-aminopyridin-3-yl)methyl);

one of R^3 and R^4 is (indol-3-yl)CH_2 optionally substituted by halo or hydroxy; and the other is benzyl (optionally substituted by halo or hydroxy) or C_4 alkyl (such as $CH(CH_3)CH_2CH_3$ or $CH_2CH(CH_3)_2$);

or R^3 and R^4 are both methyl;

R^5 and R^6 are, independently, C_{1-6} alkyl (for example CH_3, $CH(CH_3)_2$, $CH(CH_3)CH_2CH_3$ or $CH_2CH(CH_3)_2$);

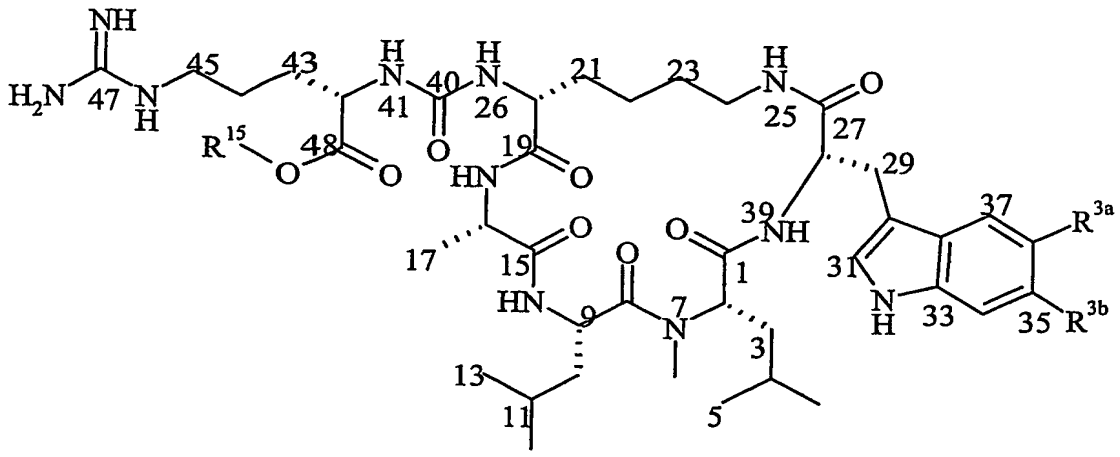
R^7, R^8, R^9, R^{11}, R^{12}, R^{13} and R^{14} are H;

R^{10} is C_{1-4} alkyl; and,

R^{15} is H or C_{1-4} alkyl.

5. A compound as claimed in any one of claims 2 to 4 wherein X is $(CH_2)_4$.

6. A compound as claimed in any one of claims 2 to 5 wherein R^1 is CO_2R^{15} in which R^{15} is H or C_{1-4} alkyl.
7. A compound as claimed in any one of claims 2 to 6wherein R^2 is straight-chain C_{1-6} alkyl substituted at its terminus by NH_2, $CNH(NH_2)$ or $NHCNH(NH_2)$; C_4 alkyl (such as $CH(CH_3)CH_2CH_3$ or $CH_2CH(CH_3)_2$); or (aminopyridinyl)methyl.
8. A compound as claimed in any one of claims 2 to 4 wherein R^2 is C_{1-6} alkyl ($CH(CH_3)CH_2CH_3$ or $CH_2CH(CH_3)_2$), benzyl, or straight-chain C_{1-6} alkyl substituted at its terminus by NH_2, $CNH(NH_2)$, $NHCNH(NH_2)$ or (6-aminopyridin-3-yl)methyl.
9. A compound as claimed in any one of claims 2 to 8 wherein R^2 is straight-chain C_{1-6} alkyl substituted at its terminus by NH_2, $CNH(NH_2)$, $NHCNH(NH_2)$ or (6-aminopyridin-3-yl)methyl.
10. A compound as claimed in any one of claims 2 to wherein R^3 is CH_2indolyl (wherein the indolyl is optionally substituted by one or more of: halogen or hydroxy, C_{1-4} alkyl or benzyl (optionally substituted by halogen or hydroxy).
11. A compound as claimed in any one of claims 2 to 10 wherein R^4 is CH_2indolyl (wherein the indolyl is optionally substituted by one or more of: halogen or hydroxy, C_{1-6} alkyl ($CH(CH_3)CH_2CH_3$ or $CH_2CH(CH_3)_2$) or benzyl (optionally substituted by halogen or hydroxy.
12. A compound as claimed in any one of claims 2 to 11 wherein R^5 and R^6 are, independently, C_{1-6} alkyl (such as methyl, iso-propyl, $CH(CH_3)CH_2CH_3$ or $CH_2CH(CH_3)_2$).
13. A compound as claimed in any one of claims 2 to 12 wherein R^7, R^8, R^9, R^{11}, R^{12}, R^{13} and R^{14} are all H.
14. A compound as claimed in any one of claims 2 to 4 wherein R^{10} is C_{1-4} alkyl.
15. A compound as claimed in claim 2 which is a compound of the following formula



in which

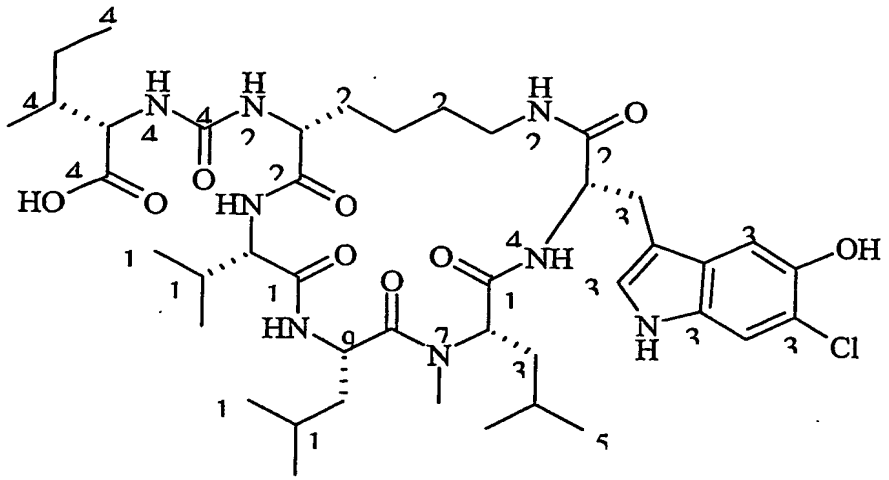
R^{3a} is H, R^{3b} is H and R^{15} is H;

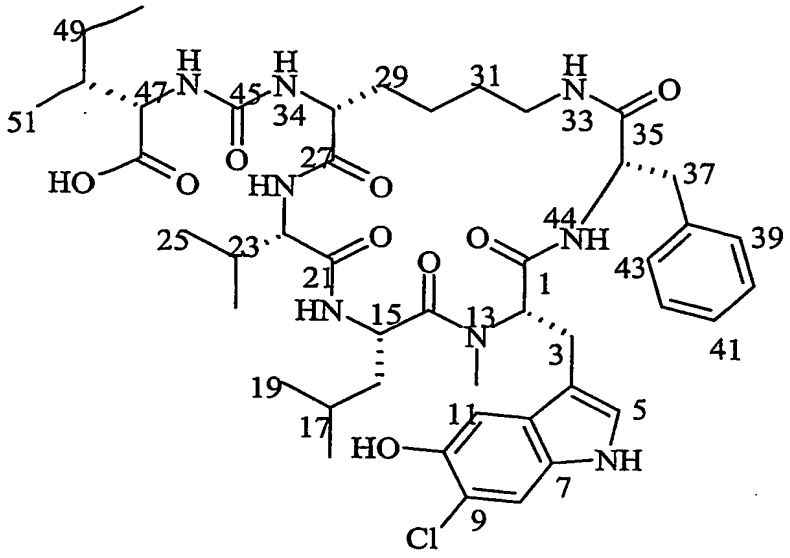
R^{3a} is OH, R^{3b} is Cl and R^{15} is H;

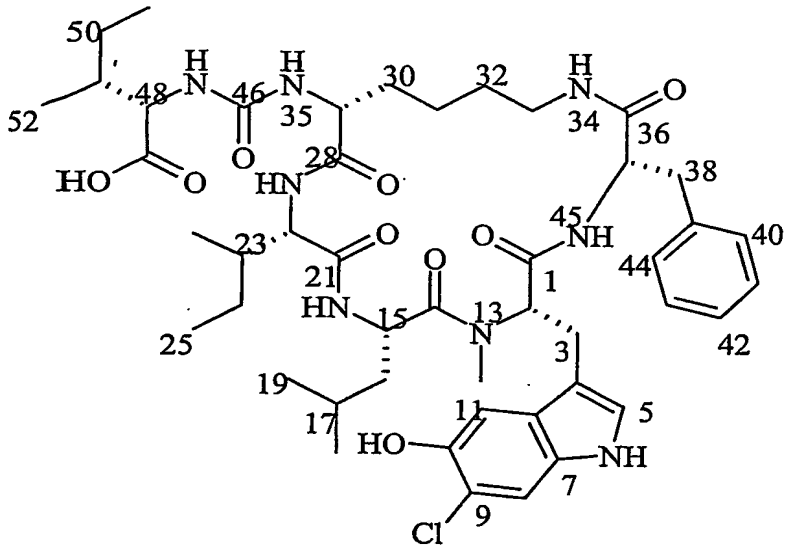
R^{3a} is OH, R^{3b} is Cl and R^{15} is CH_3;

R^{3a} is H, R^{3b} is H and R^{15} is CH_3;

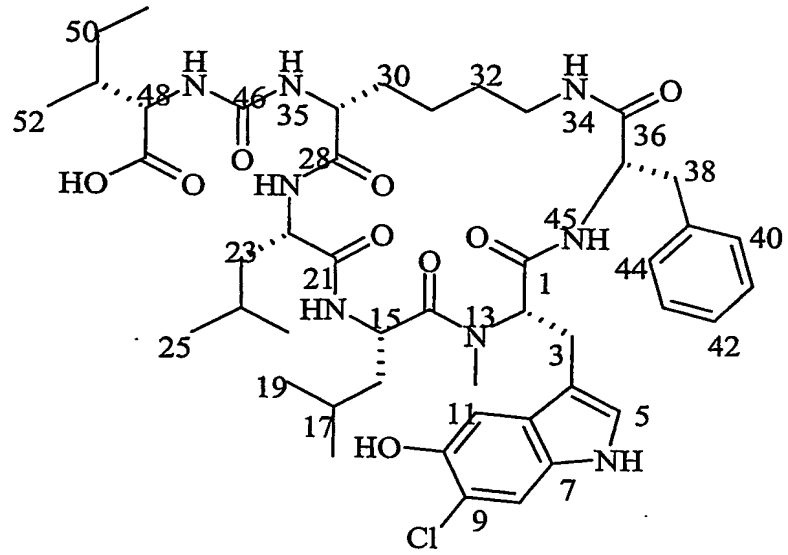
R^{3a} is H, R^{3b} is Cl and R^{15} is H;

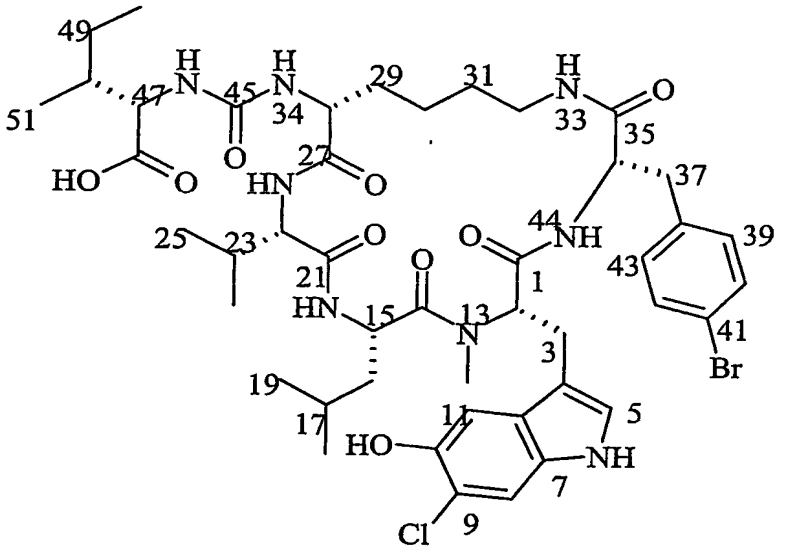


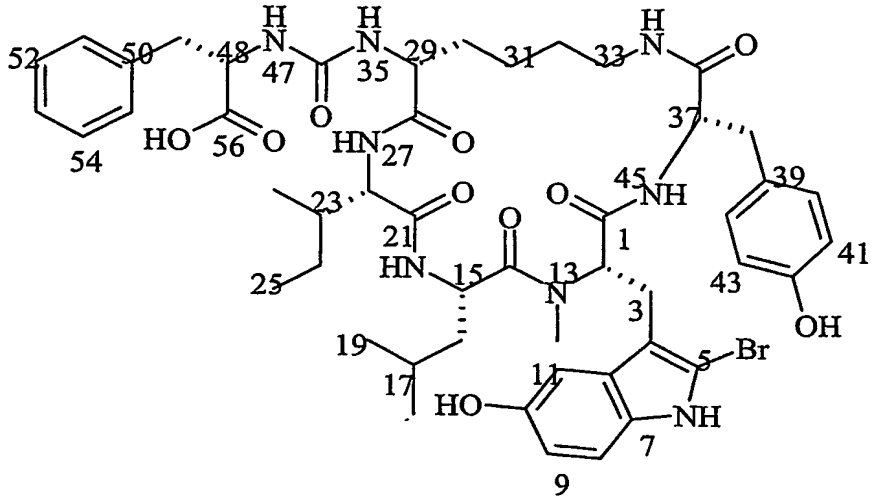


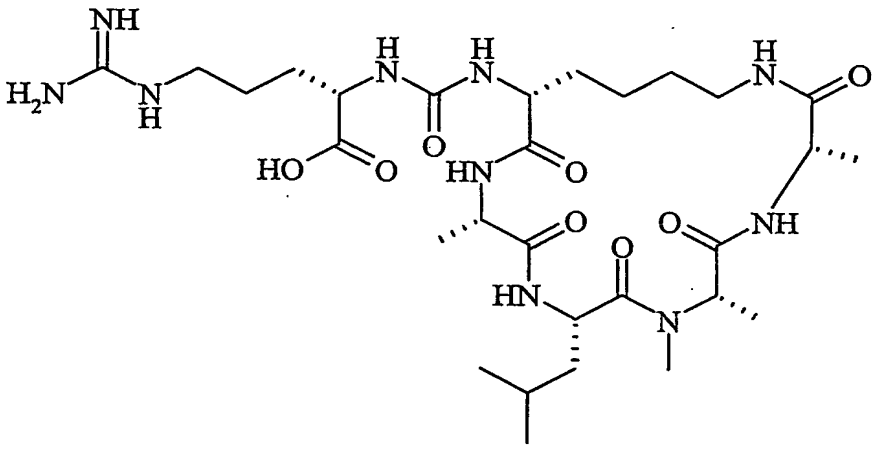


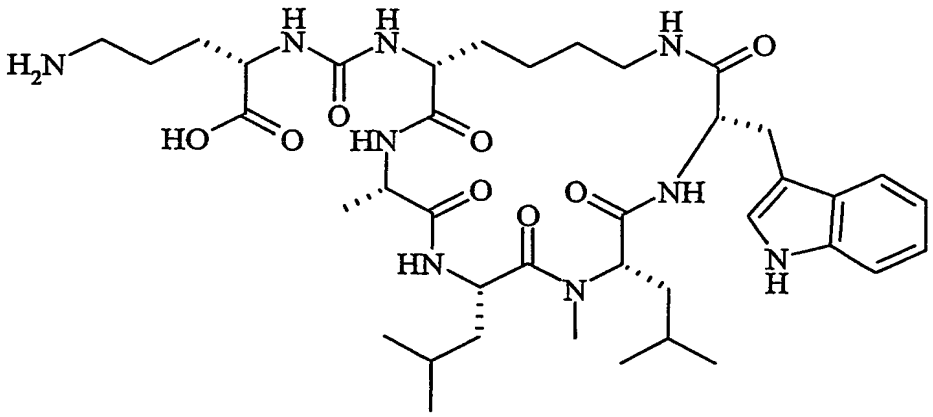
5

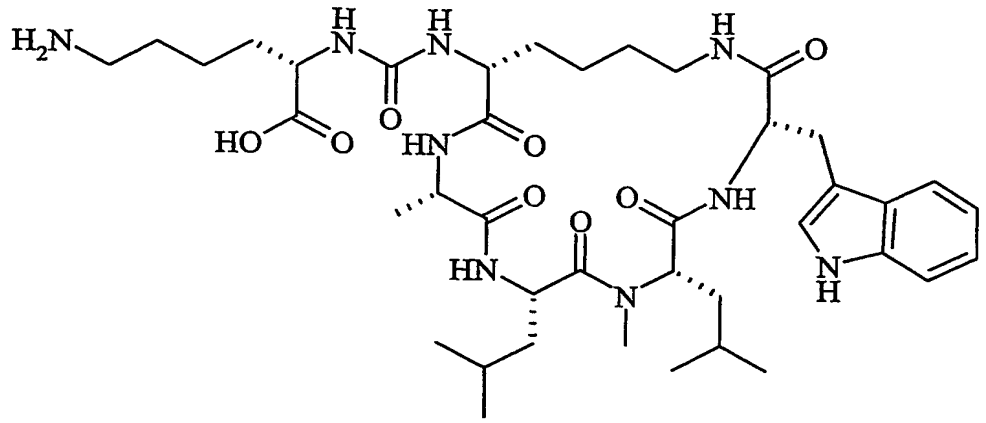

50
52
48
46
35
30
32
34
36
38
HO
O
HN
28
O
45
NH
40
44
23
21
O
1
25
HN
15
13
N
3
42
19
17
11
5
HO
NH
7
9
Cl

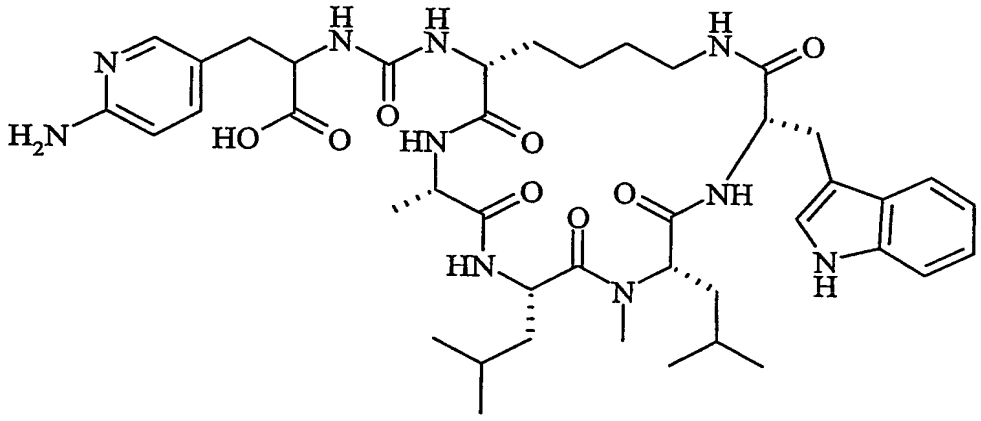

49
51
47
45
34
29
31
33
35
37
HO
O
HN
27
O
44
NH
39
25
23
21
O
1
43
HN
15
13
N
3
41
Br
19
17
11
5
HO
NH
7
9
Cl

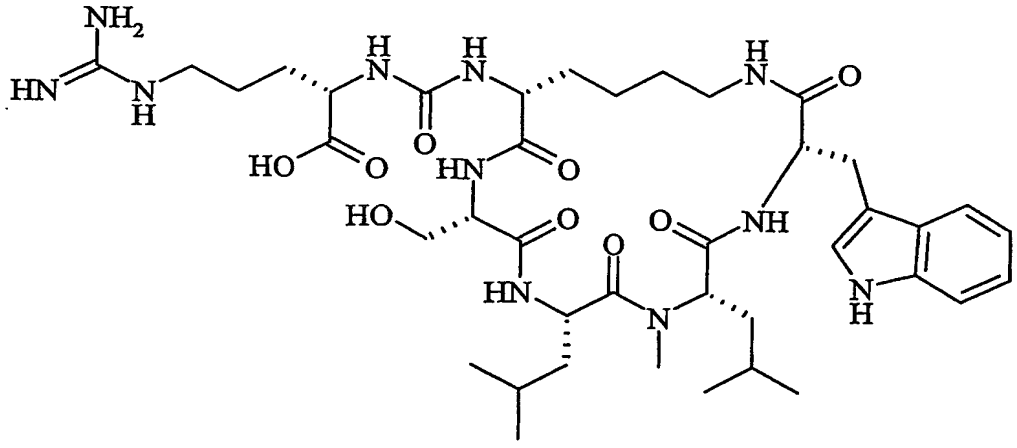












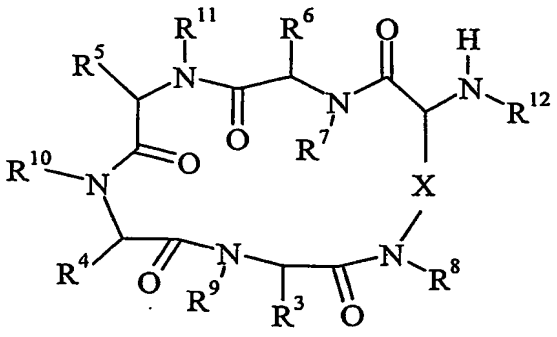
or a pharmaceutically acceptable salt or solvate thereof, or a solvate of a pharmaceutically acceptable salt thereof.

16. The use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt; as claimed in any one of claims 2 to 15 in a method of manufacturing a medicament for the treatment or prophylaxis of a condition wherein inhibition of carboxypeptidase U is beneficial.

17. The use as claimed in claim 16 for the manufacture of a medicament for the treatment or prophylaxis of thrombosis and/or hypercoagulability in blood and/or tissues; atherosclerosis; fibrotic conditions; inflammatory diseases; or a condition which benefits from maintaining or enhancing bradykinin levels in the body of a mammal (such as man).

18. A pharmaceutical formulation containing a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt; as claimed in any one of claims 2 to 15 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

19. A compound of formula

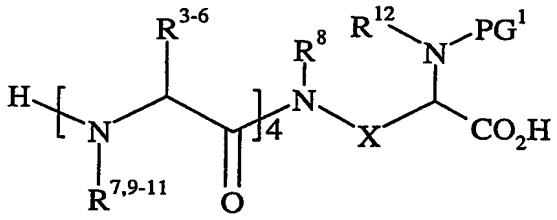


(VII)

wherein R^3 to R^{12} and X are as defined in any one of claims 1 to 14

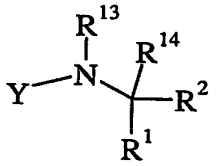
20. A process for preparing a compound as claimed in claim 19 which comprises treating a compound of formula VI in which PG1 is a suitable protecting group

with a peptide coupling agent in the presence of a non-nucleophilic base in a polar aprotic solvent and then removing the protecting group.



(VI)

21. A process for preparing a compound of formula I as claimed in any one of claims 2 to 17 which comprises reacting a compound of formula VII as defined in claim 19 with a compound of formula VIII



(VIII)

in which Y is an activated ester or NY is an isocyanate group.